A five-year retrospective review of fatalities involving novel psychoactive substances in Southern Ireland

ANDREW MAZUREK[1], MARGOT BOLSTER[2]

Abstract

INTRODUCTION: Novel psychoactive substances (NPS) are rapidly emerging and being reformulated to evade legislative controls, creating unpredictability in drug markets and ineffective drug policies. Given that Ireland has the highest self-reported NPS use within Europe and literature regarding health risks is lacking, the *National Advisory Committee on Drugs* has advocated for the surveillance of regional trends.

OBJECTIVES: To elucidate the demographic and autopsy findings of fatal cases involving NPS in Southern Ireland as compared to deaths involving traditional drugs of abuse (TDOA).

METHODS: Post-mortem reports from the Cork-Kerry region with positive toxicology for illicit substances between 2012-2016 were retrospectively analyzed to compare NPS and TDOA cases with respect to circumstances surrounding death, toxicological results, and pathological findings.

RESULTS: Between 2012-2016, there were 164 cases involving illicit substances in the Cork-Kerry region. NPS accounted for 17 (10.4%) cases, with an average annual mortality rate of 34.8 per 100,000 population. NPS contributed to the cause of death in 70.6% of cases where detected, compared to 43.5% for TDOA only. In both cohorts, fatal abusers were predominantly young males. Importantly, cases involving NPS showed a higher proportion of mono-drug intoxication and presentation to hospital prior to death. Autopsy findings were non-specific but commonly featured pulmonary congestion, aspiration, and cerebral oedema.

CONCLUSION: NPS are detected in a small proportion of medicolegal autopsies but contribute significantly to acute intoxication deaths. This study highlights the need for effective drug monitoring and enforcement strategies, along with improved management of drug toxicities presenting to hospital.

[1]MB BCH BAO (HONS), HBSC.
[2]MB BCH BAO, BA, MRC PATH.

Introduction

Novel psychoactive substances (NPS) encompass those psychoactive substances not prohibited under the *United Nations Convention on Narcotic Drugs*, designed to mimic the effects of illicit drugs[1]. To circumvent legal restrictions, they are often mislabeled as 'research chemicals' or 'bath salts'. NPS are emerging and being reformulated at increasingly rapid rates, creating unpredictable drug markets and ineffective drug policies[1]. By 2021, the *EU Early Warning System on NPS* was monitoring over 830 substances with synthetic cannabinoids, synthetic cathinones and phenylethylamines among the most commonly reported[2].

EPIDEMIOLOGY

Major European monitoring centres report a low incidence of NPS in drug-related emergency presentations, between 0-2.8% monthly, with higher frequencies for traditional recreational drugs and misused prescription medications[3]. Synthetic cathinones were the most frequently encountered, particularly mephedrone and methedrone. Highly concordant across major geographic zones was the demographic profile of NPS users reporting acute toxicity: male (>75%) and under 30 years old[4-5]. Clinical presentation upon admission was predominantly neurological and psychological, with cardiovascular symptoms also present in a significant proportion of cases[4-6]. The authors have previously reviewed the common clinical symptoms associated with NPS toxicity and proposed mechanisms of action for these psychoactive substances[7].

The leading cause of death reported in forensic casework studies was acute drug toxicity, particularly with synthetic cathinones[8]. Pathological findings commonly reported were cardiac ischaemia and cerebral hypoxia, which may be explained by chronic vasoconstriction[5,8]. Traumatic injuries, including hangings and homicidal cases, were also important contributors to fatalities. Post-mortem drug concentrations vary widely in the literature, prohibiting the establishment of 'fatal ranges' for commonly encountered NPS.

IRISH PERSPECTIVE

The emergence of NPS in Ireland was noted in 2005 with the rise of 'legal highs' sold in headshops, which at the time complied with Irish law[9]. In response, the Irish government implemented two legislative controls in 2010 by i) amending the *Misuse of Drugs Act* to include NPS, and ii) introducing the *Criminal (Psychoactive Substances) Act*[10]. While regulations succeeded in curtailing headshops, availability through street and online markets has continued[11]. 'Darknet' cryptomarkets have particularly changed the model of illegal drug distribution by utilizing anonymized online transactions[12].

While significant changes to lifetime prevalence were not detected post-legislation, this period demonstrated lower rates of recent NPS use and problematic practices[13], consistent with short-term results observed elsewhere[14]. While use of all NPS categories remains higher than desired by legislators, small-scale post-legislative studies in Ireland have reported reductions in various NPS detection rates and shifts in attitudes regarding the perceived safety of these products[11,15].

Despite reduced detection rates, levels of NPS use in Ireland remain disproportionately high. In the *Youth Attitude on Drugs* report[16], Ireland had the highest self-reported NPS use at 16% prevalence, whereas most European countries reported levels under 5%. Furthermore, the national drug-induced mortality rate for adults was 71 deaths per million, over three times the European average[17]. Current literature regarding drug fatalities linked to NPS, however, is limited mainly to case reports. Despite anecdotal accounts, published data on NPS toxicity remain scarce due to the rapid emergence of novel formulations[18]. Consequently, the *National Advisory Committee on Drugs* has recommended further research into shifting patterns of drug consumption, with particular focus on the surveillance of local trends[18]. These steps would contribute to a pragmatic public health approach, critical for the development of appropriate evidence-based responses.

AIMS AND OBJECTIVES

The aim of this study was to elucidate demographic and autopsy findings of fatalities involving consumption of NPS in Southern Ireland compared with traditional illicit drugs of abuse (TDOA). Specific objectives were to: i) compare the fatality rates involving NPS toxicity with TDOA; ii) analyze demographic characteristics of fatal abusers within both cohorts; and iii) explore the common autopsy findings in NPS overdoses.

Methodology

STUDY DESIGN

A retrospective cohort analysis was conducted, reviewing all post-mortem reports completed by the Assistant State Pathologist between 2012-2016. The geographic area covered by the Assistant State Pathologist corresponds to the *Health Service Executive* Community Healthcare Organization Area 4, covering counties Cork and Kerry[19]. A total of 4129 cases were completed by the Assistant State Pathologist between 2012-2016.

Given that drug toxicity deaths are rare within the general caseload of the forensic service, with NPS constituting an even smaller fraction, the study aimed to include all deaths involving illicit substances over the 5-year period. All reports for 2012-2016 were screened to identify cases involving illicit substances, using toxicology reports and cause of death statements. Cases positive for illicit substances were reviewed in full to extract study variables.

STUDY MEASURES

Case histories, post-mortem findings and toxicological analyses were reviewed from each case to ascertain trends in demographic data and pathological findings. NPS were identified according to classification by the *European Monitoring Centre for Drugs and Drug Addiction*[20]. TDOA included cocaine, heroin, and

amphetamines/methamphetamines. Other co-ingested drugs were also recorded, however ethanol was not recorded where the report indicated decomposition as the likely source.

Demographic measures included year, sex, age, location of death, and history of drug addiction. Pathological findings included cause of death, comorbidities, and major autopsy findings. A drug-related death was defined as one in which the forensic pathologist concluded that the drug contributed to the death, directly or indirectly[21]. A direct drug death was defined as an acute overdose with the drug reported as the primary cause of death, whereas an indirect drug death was a death in which the drug significantly contributed to death but was not the primary cause.

STUDY ETHICS

This study was approved by the Clinical Research Ethics Committee of the Cork Teaching Hospitals. Written permission to access post-mortem reports was obtained from relevant coroners. Data was extracted in aggregate and identifying information pertaining to decedents were not retained.

DATA ANALYSIS

The primary analysis was descriptive, calculating the proportion of positive cases between NPS and TDOA for each categorical study variable. The mean age and standard deviation for the two groups was calculated. The average annual fatality rate was calculated using census data for Cork and Kerry counties from the Central Statistics Office[22].

Results

Between January 1, 2012 and December 31, 2016, there were 164 cases with positive toxicology for illicit substances. NPS were detected in 17 (10.4%) cases while 147 (89.6%) were positive for TDOA only. The psychoactive substances detected varied each year (*Table 1*). NPS were implicated in the cause of death in 70.6% (12/17) of cases where these substances were detected; in comparison to 43.5% (64/147) for TDOA only. The proportion of drug-related deaths for the NPS cohort (range 50-100%) was indeed equal to or higher than the TDOA cohort (range 33-50%) for each given year (*Figure 1*). All NPS cases were direct drug deaths, while 12.5% of cases with TDOA were indirect drug deaths.

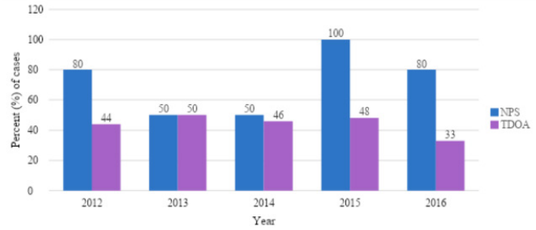

Figure 1. Proportion of cases with positive toxicology for illicit substances deemed to be a drug-related death (novel psychoactive substances (NPS) vs traditional drugs of abuse (TDOA)), per year.

DEMOGRAPHIC TRENDS

There were 68 male and 8 female drug-related deaths from 2012-2016 in the Cork-Kerry region. The gender disparity was similar in NPS and TDOA groups, with males representing 91.7% and 89.1% of cases, respectively (*Table 2*). Age at death ranged from 18-54 years (NPS: 18-42 years, TDOA: 19-54 years). The NPS group had a slightly lower mean age of 28.8 years compared to TDOA with a mean of 32.1 years.

A known history of drug addiction was recorded in 25.0% of NPS fatalities and 35.9% of TDOA fatalities. Regarding location of death, rates of death occurring in a home environment were similar between the two groups but the rate of presentation to hospital prior to death was higher in the NPS cohort (33.3%) versus the TDOA cohort (14.1%).

Table 2. Demographic characteristics of fatal abusers (NPS vs TDOA).

	NPS (n=12)	TDOA (n=64)
Gender, male	91.7%	89.1%
Age at death (years), mean ± SD	28.8 ± 8.3	32.1 ± 8.2
History of drug addiction	25.0%	35.9%
Place of death		
Home	66.7%	59.4%
Hospital	33.3%	14.1
Outdoor	--	4.7%
Other	--	20.3%
Unknown	--	1.6%

POLYSUBSTANCE USE

Polydrug intoxication was the most common scenario in both NPS and TDOA fatalities (Table 3). There was a higher rate of mono-drug overdose in the NPS group (29.4%) than for TDOA (12.5%). Most commonly co-ingested with NPS were benzodiazepines (47.1%) and amphetamines (41.2%). Amphetamines and alcohol were also found to be mixed with other drugs, though at lower frequencies.

Table 1: Novel psychoactive substances detected by toxicological analysis by year.

2012	2013	2014	2015	2016
Mephedrone PMA PMMA	MDEA Methylone PMMA	4-MEC Benzylpiperazine Mephedrone MDVP Methylone PMA PMMA	Butylone	25I-NBOMe "N-Bomb" Acetylfentanyl Fluorofentanyl Mitragynine

4-MEC: 4-methylethcathionine; MDEA: Methylenedioxyethylamphetamine; MDVP: Methylenedioxypyrovalerone; PMA: Paramethoxyamphetamine; PMMA: Paramethoxymetaphetamine

Table 3. Proportion of mono-drug intoxications and polydrug combinations detected, per drug class

Drug	Total (n)	Mono-drug overdose (%)	Proportions of mixed drugs by type (%)						
			NPS	Heroin	Cocaine	AMP	BDZ	Alcohol	Methadone
NPS	17	29.4	--	5.9	11.8	41.2	47.1	11.8	5.9
Heroin	50	4.0	2.0	--	18.0	0	88.0	42.0	28.0
Cocaine	22	18.2	9.1	40.9	--	31.8	68.2	31.8	18.2
AMP	14	7.1	50.0	0	50.0	--	64.3	--	14.3
BDZ	60		13.3	7.3	25.0	15.0	--	15.0	25.0
Alcohol	28		3.6	75.0	25.0	14.3	67.9	14.3	10.7
Methadone	17		5.9	82.4	23.5	11.8	88.2	11.8	--

AMP = amphetamines; BDZ = benzodiazepines

Table 4. Proportion of major autopsy findings in NPS overdose deaths, by organ (n=12).

Organ	Autopsy Findings	Cases (%)
Brain	Cerebral oedema	75.0
	Acute hypoxic changes	41.7
Lungs	Lungs heavy, congested and oedematous	100.0
	Trachea and major bronchi contain blood or aspirate	75.0
	No evidence of pneumonia or pleural effusion	91.7
Heart	Heart normal size and shape	91.7
	Sectioning of myocardium shows no gross evidence of disease	91.7
	Coronary arteries show no evidence of disease	100.0
Liver	Centrilobular congestion	33.3
	Mild or extensive fatty change	33.3
Overall Autopsy	No evidence of significant natural disease	100.0
	No evidence of significant injuries or trauma	91.7

AUTOPSY FINDINGS IN NPS OVERDOSE FATALITIES

A general pattern of autopsy findings emerged within NPS overdose fatalities (*Table 4*). The brain commonly displayed generalized oedema while lungs were congested and oedematous. The trachea and major bronchi often contained blood or other aspirated material. The heart was grossly and histologically normal in almost all cases, while the overall autopsy failed to demonstrate any significant natural disease or trauma.

Discussion

Despite an overall low number of 12 NPS cases detected in post-mortem toxicology screens over the five-year period, there was great variability in the classes of NPS detected. This reflects the accelerated speed at which NPS are emerging, resulting in legislation which struggles to adapt. There have been positive developments, however, with 2016 marking a significant decrease in new synthetic cannabinoids and cathinones reported[20]. This may reflect the sustained deterrent efforts by European states and efforts abroad to close laboratories producing these substances.

While the emergence of new compounds may have slowed, 2016-2017 saw a large increase in the availability of synthetic opioids, particularly fentanils, throughout Europe[23]. These trends are reflected in the Cork-Kerry data with the emergence of acetylfentanyl and fluorofentanyl in this period. This is a concerning trend identified in the region given the highly potent nature of synthetic opioids and risk of respiratory depression[24].

According to a systematic review of synthetic cathinones and

cannabinoids, acute toxicity is the leading cause of NPS fatalities[8]. This risk profile is reflected in the region as 70.6% of NPS detected were implicated in the cause of death. Furthermore, all cases were deemed a direct drug death, unlike for TDOA where 12.5% were indirect drug deaths. The acute risk of death linked to NPS has not yet been fully explained in the literature. Proposed explanations involve their increased potential for monoamine uptake blockade, which significantly increases the risk of respiratory depression[24]. This increased risk of mortality may also explain why NPS represented 10.4% of illicit substance detections when general population surveys report prevalence rates around 1%[8]. Of course, concomitant use of other drugs in this and other studies limits any definitive implication as to the exact risk profile of NPS. There is also potential that TDOA are more prevalent within the general population, making individuals better aware of non-toxic consumption levels.

Polysubstance use was implicated in 75% of NPS-related fatalities, a figure concordant with national Irish data[25]. International studies likewise demonstrate polysubstance rates of 71-92% in fatal overdoses[26]. High rates of benzodiazepine co-ingestion with all other drug categories are a concerning trend which has been consistently raised. In fact, benzodiazepine use in opioid-dependent patients has been correlated with more severe drug abuse[26]. This study thus supports continued efforts to address benzodiazepine abuse, particularly in at-risk individuals with a history of drug addiction.

DEMOGRAPHIC PROFILE OF NPS USE IN IRELAND

The 9:1 male-to-female ratio within both NPS- and TDOA-related deaths is in keeping with published literature[28]. The

underlying reason is one which begs further explanation as Irish data indicates the proportion of females entering treatment for illicit substances ranges from 19-37%[28]. Theories that male drug abusers are more likely to engage in harmful behaviours do not fully explain this study as all NPS-related deaths were direct drug deaths, without traumatic injuries.

While the age range for fatal NPS abusers in this study ranged from 18-42 years, recent data indicates that NPS use remains prevalent among adolescents and further educational efforts are required for this vulnerable population. NPS use by Irish teenagers aged 15-16 was 5% in a recent survey, placing Ireland within the top five European countries[29].

The finding that a greater proportion of NPS overdoses initially present to hospital indicates there may be opportunity for better recognition and/or management of NPS toxicities in emergency departments. Utilization of urine dipstick screens which detect commonly encountered NPS is recommended, especially when the history or physical examination is unclear, uncorroborated, or raises suspicion of drug intoxication. Such dipstick screens are available commercially but not currently implemented in the Cork-Kerry region. While antidote medications are not currently available for NPS toxicity, early recognition of NPS involvement can help prioritize the initiation of supportive measures or admission to intensive care, steps which require timely implementation to prevent irreversible or fatal consequences.

THE ROLE OF TOXICOLOGY IN NPS-RELATED FATALITIES

This study emphasizes the importance of toxicology testing, including NPS screening, in autopsies without significant natural disease or trauma. Recognition of the constellation of autopsy findings most often observed in drug-related fatalities is important for forensic pathologists as it can highlight the role of toxicological analysis, even if other co-morbidities are present. Pertinent demographic factors including male gender, young age, and history of drug addiction can further strengthen the rationale for toxicology.

While literature pertaining to NPS fatalities is limited mainly to case reports, a retrospective analysis of 61 autopsy cases involving synthetic cathinones and cannabinoids was conducted by Ezaki and colleagues[30]. Similar findings of cerebral hypoxia and pulmonary aspiration were recorded although at lower rates than for the present study. Other retrospective studies involving NPS autopsy cases have tended to focus on the methodological principles of toxicological testing used for NPS detection[31].

STRENGTHS AND LIMITATIONS

The use of post-mortem reports as the source of data confers certain limitations which need to be considered. Fatalities are a limited measure of overall health risk, representing a small, but serious, part of the spectrum of adverse effects which can occur with illicit substance use. The data analyzed relies upon the interpretation of the forensic pathologist in providing an accurate assessment as to the cause of death, an area which can be challenging when NPS are involved. Furthermore, the occurrence of post-mortem effects such as drug degradation and redistribution, can vary between cases and is not fully understood for NPS. The high level of polysubstance use was a confounding variable which prevented statistical analysis and creates difficulty in determining which agents directly contributed to death. Further, the inference of causality is restricted by the retrospective nature of the study. The small number of NPS cases retrieved in the study period limits the generalizability of the findings outside of the geographic focus of the study.

It is important to recognize that due to economic restraints, toxicological testing is not performed on all post-mortem cases but selected according to case history and autopsy findings. It is possible the number of NPS cases is underestimated in this study, as some cases without toxicological analysis could potentially reveal NPS involvement. Further, toxicology screens are only able to detect substances for which the State Laboratory has reference samples, so certain formulations may elude these drug screens.

Allowing for these limitations, the study is nonetheless able to provide regionally-focused data on the health risks of NPS abuse. The geographic focus allows for detection of trends specific to the Cork-Kerry region and inclusion of all cases with positive toxicology results for illicit substances allows for a representative picture of the prevalence and variety of NPS and TDOA being fatally abused by Cork-Kerry residents without unintended sampling bias. The reports were completed by one forensic pathologist, limiting variability in reporting and toxicological interpretations. Additionally, the State Laboratory has implemented an NPS Analytical Strategy – for which it was awarded a Civil Service Excellence and Innovation Award – lending credibility to the toxicological analyses. This project required minimal cost and labour, making it feasible for future replication.

Conclusions

Knowledge of trends in NPS prevalence and toxicity are important considerations to the development of effective and proactive drug monitoring or enforcement strategies. Dissemination of this data is important for healthcare professionals, particularly emergency physicians and forensic pathologists, in order to make accurate medical assessments. Future directions for research include establishment of the pathological processes linked to individual NPS and addressing the possibility of genetic vulnerability to NPS overdose.

This study has provided an improved understanding of the vulnerable populations and health risks specific to this demographic region. NPS are involved in a small fraction of autopsy cases but contribute significantly to acute intoxication fatalities, especially when polydrug ingestion is implicated. It remains to be seen what effects targeted efforts at drug enforcement may have on the prevalence of NPS use in Ireland and rates of drug-related fatalities.

References

1. O'Neill C. Novel psychoactive substances: risks and harms. *Community Pract.* 2014 Aug;87(8):45-7.
2. The European Monitoring Centre for Drugs and Drug Addiction. *European Drug Report: Trends and Developments. Luxembourg*: Publications Office of the European Union, 2021.
3. Dines AM, Wood DM, Yates C, et al. Acute recreational drug and new psychoactive substance toxicity in Europe: 12 months data collection from the European Drug Emergencies Network (Euro-DEN). *Clin Toxicol.* 2015 Oct;53(9):893-900.
4. Hondebrink L, Nugteren-van Lonkhuyzen JJ, Van Der Gouwe D, Brunt TM. Monitoring new psychoactive substances (NPS) in The Netherlands: data from the drug market and the Poisons Information Centre. *Drug Alcohol Depend.* 2015 Feb;147:109-15.
5. Kamijo Y, Takai M, Fujita Y, Sakamoto T. A multicenter retrospective survey of poisoning after consumption of products containing novel psychoactive substances from 2013 to 2014 in Japan. *Am J Drug Alcohol Abuse.* 2016 Sep;42(5):513-9.
6. Murray DB, Potts S, Haxton C, Jackson G, Sandilands EA, Ramsey J, et al. 'Ivory wave' toxicity in recreational drug users; integration of clinical and poisons information services to manage legal high poisoning. *Clin Toxicol.* 2012 Feb;50(2):108-13.
7. Mazurek A, Bolster M. Trends in Novel Psychoactive Substance Use and the Impact of Irish Legislative Efforts. *UCC Student Medical Journal.* 2020 Oct;1:55-63.
8. Ezaki J, Ro A, Hasegawa M, Kibayashi K. Fatal overdose from synthetic cannabinoids and cathinones in Japan: demographics and autopsy findings. *Am J Drug Alcohol Abuse.* 2016 Sep;42(5):520-9.
9. Van Hout MC. The Dynamic Landscape of Novel Psychoactive Substance (NPS) Use in Ireland: Results from an Expert Consultation. *Int J Ment Health Addiction.* 2017 Oct;15(5):985-92.
10. Ryall G, Butler S. The great Irish head shop controversy. Drugs: Educ Prev Polic. 2011 Aug;18(4):303-11.
11. Van Hout MC, Brennan R. Curiosity killed M-Cat: A post-legislative study on mephedrone use in Ireland. *Drugs: Educ Prev Pol.* 2012;19(2):156-62.
12. Pergolizzi JV, LeQuang JA, Taylor R, Raffa RB. The "Darknet": The new street for street drugs. J Clin Pharm Ther. 2017 Dec;42(6):790-2.
13. Smyth BP, James P, Cullen W, Darker C. "So prohibition can work?" Changes in use of novel psychoactive substances among adolescents attending a drug and alcohol treatment service following a legislative ban. *Int J Drug Policy*. 2015 Sep;26(9):887-9.
14. Loeffler G, Craig C. The effect of legal bans on poison control center contacts regarding 'legal highs'. *Addiction*. 2013 Jul;108(7):1348-9.
15. Van Hout MC, Bingham T. "A costly turn on": patterns of use and perceived consequences of mephedrone based head shop products amongst Irish injectors. *Int J Drug Policy.* 2012 May;23(3):188-97.
16. The Gallup Organization. Youth attitudes on drugs. Luxembourg: European Commission, 2011.
17. European Monitoring Centre for Drugs and Drug Addiction. *Ireland: Country Drug Report 2017*. Luxembourg: Publications Office of the European Union, 2017.
18. Kelleher C, Christie R, Lalor K, Fox J, Bowden M, O'Donnell C. An overview of new psychoactive substances and the outlets supplying them. Dublin: National Advisory Committee on Drugs, 2011.
19. Health Service Executive. *CHO Report Chapter 1: Executive Summary.* Dublin, Ireland: Community Healthcare Services, 2013.
20. The European Monitoring Centre for Drugs and Drug Addiction. *Early Warning System on NPS.* Lisbon, Portugal: European Union, 2019.
21. Markovic M, Kocovski L, Fernandes JR. Retrospective analysis of oxycodone- and cocaine-related deaths in Southwestern Ontario during 2003-2010. *Acad Forensic Pathol.* 2014;4(2):220-5.
22. StatBank. *Population at Each Census from 1841 to 2016 by County, Sex and Census Year.* Cork, Ireland: Central Statistics Office, 2018.
23. European Monitoring Centre for Drugs and Drug Addiction. *Fentanils and synthetic cannabinoids: driving greater complexity into the drug situation.* Luxembourg: Publications Office of the European Union, 2018.
24. White JM, Irvine RJ. Mechanisms of fatal opioid overdose. Addiction 1999;94:961-72.
25. National Drug-Related Deaths Index. *Drug-related deaths and deaths among drug users in Ireland.* Dublin: Health Research Board, 2015.
26. Backmund M, Meyer K, Meyer K, et al. Co-consumption of benzodiazepines in heroin users, methadone-substituted and codeine-substituted patients. *J Addict Dis.* 2006;24(4):17-29.
27. Hickman M, Carrivick S, Paterson S. London audit of drug-related overdose deaths: characteristics and typology, and implications for prevention and monitoring. *Addiction* 2006;102:317-23.
28. European Monitoring Centre for Drugs and Drug Addiction. *Ireland: Country Drug Report 2019*. Luxembourg: Publications Office of the European Union, 2019.
29. European Monitoring Centre for Drugs and Drug Addiction. *ESPAD Report 2015: Results from the European School Survey Project on Alcohol and Other Drugs.* Luxembourg: Publications Office of the European Union, 2015.
30. Ezaki J, Ro A, Hasegawa M, Kibayashi K. Fatal overdose from synthetic cannabinoids and cathinones in Japan: demographics and autopsy findings. *Am J Drug Alcohol Abuse* 2016;42(5):520-9.
31. Marinetti LJ, Antonides HM. Analysis of synthetic cathinones commonly found in bath salts in human performance and postmortem toxicology: method development, drug distribution and interpretation of results. *J Anal Toxicol.* 2013;37:135-46.